Clinical research informed consent form for a patient's relative

Title of the study: Characterization of esophageal motility functions and evaluation of prokinetic effectiveness in mechanically ventilated critically ill patients: high-resolution manometry study

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Contact: +420 377 103 322, +420 377 103 165

Patient: .....

Identification number: .....

Dear Sir, dear Madam,

At this point, your close relative is in a life-threatening condition that required admission to the intensive care unit and respiratory support. With your permission, we would like to offer him/her participation in the above-mentioned study. The aim of this study is to assess the degree of esophageal movement impairment, which often accompanies critically ill patients and the effect of a commonly used drug (metoclopramide) on this disorder.

Impaired motility and weakening of the lower esophageal sphincter with backflow of gastric content into the esophagus affects 50-60% of critically ill patients on mechanical ventilation and the cause of this is unclear. The consequences of this disorder are poor intake of nutrition administered through a tube into the stomach and its backflow to the esophagus, deterioration of nutritional status, easier microbial colonization of the stomach, higher risk of gastric mucosal damage and possibly aspiration of gastric content into the lungs with development of pneumonia. These consequences lead to longer hospital stays and higher mortality. One of the possible solutions to this problem is the administration of a drug to improve motility of the esophagus and stomach - metoclopramide. In critically ill patients, metoclopramide improves gastric emptying, but the effect on the esophagus and the ability to prevent backflow of gastric contents to the esophagus and possibly to the lungs has not been studied.

Patients are selected for participation in the study according to the inclusion criteria: age over 18 years, respiratory failure with the need for mechanical ventilation and the need to administer artificial nutrition through a tube into the stomach with or without obvious difficulty in receiving this nutrition, as the backflow of nutrition to the esophagus may occur in both cases. In selected patients, esophageal motility and stomach-to-esophagus fluid backflow are continuously monitored for 6 hours using a special, 3mm wide catheter, which is inserted through the nose into the stomach together with a commonly used feeding tube, which is used in all patients with this degree of illness. In the middle of the 6-hour interval, a single dose of

metoclopramide is given into a vein to patients who show abnomal esophageal sphincter tightness, or have episodes of fluid backflow in the first three hours, or are who show signs of impaired gastric motility and thus limited nutritional intake. At the same time, clinical parameters of vital functions will be recorded and blood samples will be taken for laboratory examination. These samples overlap with standard samples, which are taken as part of routine monitoring of critically ill patients. Therefore, they do not impose an unnecessary burden on the patient.

How does the study benefit the patient?
During this study, we will be able to find out whether your relative's treatment with metoclopramide works not only to improve gastric motility (usual indication) but also to prevent backflow of gastric contents to the esophagus or airways (as yet unknown data). The obtained data can help optimize the treatment of the ongoing disease, or by adjusting the nutritional regime and its administration prevent the development of pneumonia, which can complicate mechanical ventilation.

What are the potential risks from the study?

1/ Any discomfort resulting from nasal catheter insertion will be addressed by administering a small dose of sedative or by catheter insertion in the early morning if sedatives are administered to induce night sleep. The catheter is thin and soft so any injury to the nose or nasopharynx during insertion is unlikely though it cannot be completely ruled out.

2/ The risk of administering 1 dose of metoclopramide 10 mg into a vein is very small. With the usual therapeutic doses of metoclopramide, side effects are rare and mild and transient. The development of side effects depends on the dose and the overall duration of treatment. Fatigue, drowsiness, restlessness may occur frequently (approximately 10% of patients). Uncommonly, insomnia, headache, confusion, dizziness or mental depression, indigestion, urticaria and dry mouth may occur. Rarely (0.2% of patients), extrapyramidal side effects occur and, in most cases, manifest as acute dystonia. Symptoms may include involuntary movements of the limbs and facial muscles, torticollis, ocular crisis, tongue crawling, trismus, bulbar type speech, opisthotonus, and in rare cases, stridor with dyspnoea. These reactions occur mainly in younger women, in whom the daily dose of metoclopramide is between 30 and 40 mg. The risk of extrapyramidal side effects is reduced if the total daily dose of metoclopramide does not exceed 0.5 mg / kg body weight, i.e. 35 mg / day in a 70 kg human. Symptoms consistent with parkinsonism and tardive dyskinesia may occur, especially in elderly patients who are taking higher doses over a long period of time. Haematological disorders, hypersensitivity reactions, neuroleptic malignant syndrome and urinary incontinence have been reported rarely, but again include long-term drug administration. In practice, side effects are very rarely observed in critically ill patients.

No drugs or invasive procedures out of the ordinary practice are used during this study.

All obtained results will be used anonymously and the data will be handled in accordance with the valid laws of the Czech Republic on personal data protection. If the results of the study are published, none of the included patients will be recognizable from the published data. Participation in a clinical trial can be terminated at any time without affecting further treatment and all further treatment will be

performed in a completely standard manner. Participation in this study is entirely voluntary and disagreement with participation will not adversely affect the physician relationship and further treatment. In case the condition of your relative improves, we will then contact him or her to give consent with anonymous use of the obtained data for publication purposes. If you have any further questions or concerns after reading this information, your questions will be answered at any time.

I attest that the above facts have been communicated and explained to me by the doctor, that I have understood them and that I have had the opportunity to ask additional questions which have been answered by the doctor. By signing this document, I declare that I understand its content and that I agree to the inclusion of my relative in the study and to the anonymous processing and publication of data obtained during the study.

Name of relative: ……..

Relation to patient: …….

Signature of relative: .....

Signature and name of informing doctor: ....……

In Pilsen, date: …… time: ……..

Clinical research informed consent form for a patient

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Contact: +420 377 103 322, +420 377 103 165

Patient: .....

Identification number: .....

Dear Sir, dear Madam,

You are now recovering from a serious condition that required admission to the intensive care unit and temporary or possibly ongoing respiratory support. We would like to inform you that you have been included in the above-mentioned study. Due to the fact that your medical condition did not allow you to consent before inclusion in the study (after meeting all entry requirements), one of the inclusion criteria is the need of respiratory support with mechanical ventilation, the consent of your close relative was obtained initially.

What is the purpose of this study?
The aim of this study is to assess the degree of esophageal movement impairment, which often accompanies critically ill patients and the effect of a commonly used drug (metoclopramide) on this disorder. Impaired motility and weakening of the lower esophageal sphincter with backflow of gastric content into the esophagus affects 50-60% of critically ill patients on mechanical ventilation and the cause of this is unclear. The consequences of this disorder are poor intake of nutrition administered through a tube into the stomach and its backflow to the esophagus, deterioration of nutritional status, easier microbial colonization of the stomach, higher risk of gastric mucosal damage and possibly aspiration of gastric content into the lungs with development of pneumonia. These consequences lead to longer hospital stays and higher mortality. One of the possible solutions to this problem is the administration of a drug to improve motility of the esophagus and stomach - metoclopramide. It is a commonly used drug in this setting and it improves gastric motility, but the effect on the esophagus and the ability to prevent backflow of gastric contents into the esophagus and possibly into the lungs has not been studied.

How is the study performed?
Patients are selected for participation in the study according to the inclusion criteria: age over 18 years, respiratory failure with the need for mechanical ventilation and the need to administer artificial nutrition through a tube into the stomach with or without obvious difficulty in receiving this nutrition, as the backflow of nutrition to the esophagus may occur in both cases. In selected patients, esophageal motility and stomach-to-esophagus fluid backflow are continuously monitored for 6 hours using a special, 3mm wide catheter, which is inserted through the nose into the stomach

together with a commonly used feeding tube, which is used in all patients with this degree of illness. In the middle of the 6-hour interval, a single dose of metoclopramide is given into a vein to patients who show reduced esophageal sphincter tightness, or have episodes of fluid backflow in the first three hours, or are who show signs of impaired gastric motility and thus limited nutritional intake. At the same time, clinical parameters of vital functions will be recorded and blood samples will be taken for laboratory examination. These samples overlap with standard samples, which are taken as part of routine monitoring of critically ill patients. Therefore, they do not impose an unnecessary burden on the patient.

How does the study benefit the patient?
During this study, we are able to determine whether metoclopramide treatment works not only to improve gastric motility (usual indication) but also to prevent backflow of gastric contents to the esophagus or airways (as yet unknown data). The obtained data can help optimize the treatment of the ongoing disease, or by adjusting the nutritional regime and its administration, prevent the development of pneumonia, which can complicate mechanical ventilation.

What are the potential risks from the study?

1/ Any discomfort resulting from nasal catheter insertion will be addressed by administering a small dose of sedative or by catheter insertion in the early morning if sedatives are administered to induce night sleep. The catheter is thin and soft so any injury to the nose or nasopharynx during insertion is unlikely though it cannot be completely ruled out.

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I attest that the above facts have been communicated and explained to me by the doctor, that I have understood them and that I have had the opportunity to ask additional questions which have been answered by the doctor. By signing this document, I declare that I understand its content and that I agree to the anonymous processing and publication of data obtained during the study.

Name of the above-mentioned patient: ……..

Signature and name of informing doctor: ....……

In Pilsen, date: …… time: ……..